RFP-NIAID-DMID-NIHAI2017089
Amendment #2

"MANUFACTURING AND CHARACTERIZATION SERVICES FOR VACCINES AND OTHER BIOLOGICSFOR INFECTIOUS DISEASES"

Amendment Issue Date: April 28, 2017

Proposal Due Date/Time: June 7, 2017 at 12 noon EST
[Unchanged]

Issued By: Shane Ryan
Contracting Officer
OA/DEA/NIAID/NIH/DHHS

Offerors must acknowledge receipt of this Amendment on each copy of the proposal submitted. Failure to receive your acknowledgment of this Amendment may result in the rejection of your proposal.

The hour and date specified for receipt of proposals HAS NOT been extended.

This Amendment #1 is amending certain terms and conditions of the RFP as well as to provide questions and responses received in reference to RFP-NIAID-DMID-NIHAI2017089.

	Question	**DMID Response**
1	There are conflicting instructions provided for the LOE for Task Order 01. The LOE for Task Order 01 is provided as 600 hours in the Business Proposal Instructions (Attachment 5), but the SOW for Task Order 01 (Attachment 09) specifies 300 hours. Please confirm the LOE that should be utilized in cost proposals.	Please use the 300 hours in Task Order 01 (Attachment 5) – 300 hours for base and options 1-6. Do not use 600 and 200 hours as provided in the Business proposal (Attachment 5).
2	Please confirm the number of options for Task Order 01. The SOW (Attachment 09) specifies Options 1-6 will work to extend the base period. Business proposal instructions (Attachment 05) refer to Options 1-9 and provide a reduced LOE for options, although the scope described for each	Please use Option 1-6 as described in the Task Order 01 (Attachment 5). Do not use Options 1-9 as described in the business proposal (Attachment 5).

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	year would be the same. Please clarify the number and scope of the Options to Task Order 01.	
3	Attachment 05 Business Instructions specify the yearly activities estimated per Task Area. Is the Offeror expected to multiply estimated costs for STO 1-4 per these yearly estimates? If so, how should STO costs be divided across Task Areas for those that fall within scope of several areas, i.e. STO 3 & 4?	Attachment 05 Business Instructions provides instructions for cost estimates for Task Orders 1-2 and Sample Task Orders 3-4. In addition, the Table on page 108 should be used to create a single budget with line items as provided in the table. Provide a budget only for these items and assume all items are fully awarded within that year. Note that the estimated number of awards are for single projects such as 1 year of Task Area A, Administrative & Technical Management; Task Area B, 5 Product Development Plans; Task Area C, 4 Product Screening, Optimization, Construction & Process Development projects; Task Area D, 3 Master Cell Banks; Task Area E, Quality & Regulatory Management & Support including 1 DS/DP project, and 2 audits.
4	Attachment 3 Statement of Work indicates Task Area C includes process development for "vaccines, vaccine components, other biologics, and critical reagents." However, the Technical Proposal Instructions (Attachment 4) identify the general Task Area C as Recombinant Protein Vaccine Development. Please confirm the general Task Area C includes both viral and protein products.	Technical Proposal Instructions (Attachment 4), Section 3, bullet 3 "Task Area C: Recombinant Protein Vaccine Development" should be modified to "Task Area C: Product Screening, Optimization, Construction, and Process Development."
5	STO 3: Under the BASE, should Offerors assume plasmid(s) reagents from the requestor are suitable to support the initial expression/purification studies, or should optimization of the plasmids be built into the plan and cost?	The offeror should assess the entire Sample Task Order, identify assumptions, determine the best path forward, provide rationale, and then provide the proposal based on this assessment. The offeror should include costs as appropriate.

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6	STO 3 - OPTION 1: Is it correct to assume the objective of purification development for this option is to result in a GMP-compliant and scalable process, or is objective to obtain the best purification recovery regardless of the method, i.e. should the HIS tag be replaced at this point in development or later?	The offeror should assess the entire Sample Task Order, identify assumptions, determine the best path forward, provide rationale, and then provide the proposal based on this assessment. The offeror should include costs as appropriate.
7	STO 4: - BASE: It is not clear if the final formulated product should be in liquid form or lyophilized form. Lyophilization studies are mentioned here but not in the options.	STO 4, Based, section 2.b should state: "…form for formulation studies." Please remove "and lyophilization" The offeror should assess the entire Sample Task Order, identify assumptions, determine the best path forward (lyophilization or liquid formulation), provide rationale, and then provide the proposal based on this assessment. The offeror should include costs as appropriate.
8	STO 4 - OPTIONS 2/4: Is it correct to assume that both ImV drug product ($10e^6$) and peptide adjuvant (1x) are to be formulated and filled separately and then mixed at bedside to the correct concentration of adjuvanted vaccine dose?	The offeror should assess the entire Sample Task Order, identify assumptions, determine the best path forward (separate filling versus single filling), provide rationale, and then provide the proposal based on this assessment. The offeror should include costs as appropriate.
9	STO 4 - OPTIONS 2/4: Is it correct to assume that stability studies will be performed only on the separately filled ImV drug product ($10e^6$) and adjuvant (1x) and that no stability studies are required for the final adjuvanted vaccine doses post mixing?	The offeror should assess the entire Sample Task Order, identify assumptions, determine the best path forward, provide rationale, and then provide the proposal based on this assessment. The offeror should include costs as appropriate.
10	STO4: Was a bedside mixing study performed for the previous clinical studies where the protein adjuvant was utilized? In follow up, is it assumed	The offeror should assess the entire Sample Task Order, identify assumptions, determine the best path

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	there will be sufficient quantities of peptide provided by the manufacturer at the cost provided and that no further formulation optimization will be required?	forward, provide rationale, and then provide the proposal based on this assessment. The offeror should include costs as appropriate.
11	For task orders, at what point will the discovery be tech transferred? As a Master Cell Bank or earlier in the process and if earlier, what part of the development?	The offeror should assess the entire Sample Task Order to determine the best path forward and provide a proposal based on this assessment.
12	Are audits performed by respondent limited to those necessary to execute respondents GMP obligations or will audits (Task Area E) be issued as an individual task order?	Audits may be performed within task order as a prerequisite to performing cGMP activities and audits may also be performed as a service in an individual task order.
13	Are foreign non-profits (Canada) eligible as an Offeror in response to this solicitation?	p. FAR Clause **52.225-1, Buy American--Supplies** (May 2014) is deleted in its entirety and FAR Clause **52.225-5, Trade Agreements** (October 2016) is substituted therefor. Notably, the following countries are NOT TAA eligible or compliant at this time: Russia India China Pakistan Malaysia Indonesia Iraq

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		Iran Sri Lanka
14	If so, are there any other instructions/limitations for foreign non-profits not covered in the Revised_Final_Solicitation_March_9_2017_(1).pdf?	p. FAR Clause **52.225-1, Buy American--Supplies** (May 2014) is deleted in its entirety and FAR Clause **52.225-5, Trade Agreements** (October 2016) is substituted therefor. Notably, the following countries are NOT TAA eligible or compliant at this time: Russia India China Pakistan Malaysia Indonesia Iraq Iran Sri Lanka
15.	Please elaborate on the types of vaccines and products planned for production under the RFP: • What pathogens or diseases are of particular interest? What types of live-attenuated organisms may be produced – viruses, bacteria, fungi, parasites?	The RFP Attachment 03: Parent Contract Statement of Work identifies the pathogens of interest, the types of vaccines and other biologics, and interest in adjvuants. Monoclonal antibody interest should be

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	• Is there an interest in production & characterization of mAbs or mAb-like molecules? • Are (novel) adjuvants an area of interest?	determined by assessing the definitions of "Other Biologics" and "Reagent."
16.	While in the RFP, the Biosafety levels and the maintenance of facilities that provide aseptic and/or sterile conditions is well-described, there is less clarity on the level of bio-containment that is expected for product *manufacturing* and if BSL-3 may be required. Is a BSL-3 or higher containment expected for manufacturing and product release?	Please see the definition of "Other Biologic."
17.	Will any drug product (potency) testing require *in vivo* (animal-based) assays?	The offeror should assess the entire RFP and determine if *in vivo* (animal based) assays would be required.
18.	Should applicants plan and outline long-term storage of drug product after cGMP manufacturing and release?	The offeror should describe long-term storage of drug product in the appropriate section of the proposal.
19.	In Attachment 05, page 112: While the expected number of vials per cGMP production run is outlined, there is no mention on bioreactor scale. Therefore, what is the <u>maximum</u> scale (in volume) of cGMP manufacturing that is expected? This will allow us to determine (bioreactor) capacity of our CMOs and plan our sub-contracting.	Assume downstream purification results in a final overall yield of 50%. The offeror should assess the entire Sample Task Order, identify assumptions, determine the best path forward, provide rationale, and then provide the proposal based on this assessment. The offeror should include costs as appropriate.
20.	In Attachment 07, Page 119: Will applicants sub-contracting to a CMO(s) for Process Development and cGMP manufacturing be at a disadvantage under scoring under criterion 5 (20 points)?	The proposed facilities, whether in-house or subcontracted to a CMO, will be assessed under criterion 5.

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		Change "Assess the Offeror's facility(facilities)" to "Assess the proposed facility(facilities)"
21.	In Attachment 10, sample Task order, page 138, the SCOPE outlines 'a cGMP-compliant expression system'. However, it is unclear for recombinant protein vaccine development, are there any particular expression systems of special interest (mammalian, *E. coli*, yeast)?	The offeror should assess the entire Sample Task Order, identify assumptions, determine the best path forward, provide rationale, and then provide the proposal based on this assessment. The offeror should include costs as appropriate.
22.	In Attachment 10, sample Task Order, page 140, while cGMP compliant storage of MCB for 2 years is requested, in Attachment 05 page 111, MCB storage is requested to be assumed for a duration of 2.5 years. Please help reconcile this difference.	Page 111 should state 2 years and not 2.5 years.
23.	In Attachment 3, on page 8 of the Attachment, under the description of Task Area A, the RFP states that the Scope of Work will include trainings, workshops and site audits. However the Business Proposal instructions in Attachment 5 do not provide guidance on how to budget for these activities. Please provide us with the guidance on how these activities should be budgeted for.	Attachment 05 Business Instructions provides instructions for cost estimates for Task Orders 1-2 and Sample Task Orders 2-3. In addition, The Table on page 108 should be used to create a single budget with line items as provided in the table. Provide a budget only for these items and assume all items are fully awarded within that year. Note that the estimated number of awards are for single projects such as 1 year of Task Area A, Administrative & Technical Management; Task Area B, 5 Product Development Plans; Task Area C, 4 Product Screening, Optimization, Construction & Process Development projects; Task Area D, 3 Master Cell Banks; Task Area E, Quality & Regulatory Management & Support including 1 DS/DP project, and 2 audits.

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		Do not provide estimates for training nor workshops.
24.	In Attachment 5 of the RFP, on page 2 of the Attachment, the following table is provided: (a) Please confirm that we should budget for each task area the number of task orders listed under "Estimated Number of Awards/year" in each year of the Contract, meaning Years 1 – 7 (the 7-year ordering period). (b) In order to ensure we understand exactly how many task orders we should budget for we wanted to present our understanding of the above table by taking Task Area B as an example. Based on the table above and further instructions on the period of Task Order 2 (2 years) we assume that in Year 1 we will budget for 5 Task Orders each for a 2 year period. And in Year 2 we would budget for an additional 5 Task Orders for a 2 year period and as such in Years 2 – 9 of the Contract we will have 10 Task Orders budgeted annually (5 will be in the second year and 5 in the first). Please confirm this is correct. If not please provide more guidance clarifying the expected budgeted for each Task Area. (c) Please confirm that we should budget for the same number of Task Orders in Year 7 of the Contract. Assuming we do so some task orders may be for periods beyond the 10 years anticipated for this Contract (for example, Sample Task Order 4).	Attachment 05 Business Instructions provides instructions for cost estimates for Task Orders 1-2 and Sample Task Orders 3-4. In addition, the Table on page 108 should be used to create a single budget with line items as provided in the table. Provide a budget only for these items and assume all items are fully awarded within that year. Note that the estimated number of awards are for single projects such as 1 year of Task Area A, Administrative & Technical Management; Task Area B, 5 Product Development Plans; Task Area C, 4 Product Screening, Optimization, Construction & Process Development projects; Task Area D, 3 Master Cell Banks; Task Area E, Quality & Regulatory Management & Support including 1 DS/DP project, and 2 audits.
25.	In Attachment 5, on page 3 of the Attachment, under the specific instructions for Task Order 1 we	Please use the 300 hours in Task Order 01 (Attachment 5) – 300 hours for base

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	are requested to budget level of effort at 600 hours in Year 1 and 200 hours in Options 1-9. Please elaborate on why you expect the level of effort to be significantly reduced in future years. Will the Scope of Work change?	and options 1-6. Do not use 600 and 200 hours as provided in the Business proposal (Attachment 5).
26.	In Attachment 5, on page 5 of the Attachment, we are provided with guidance on how to budget for Sample Task Order 3. When comparing the Sample Task Order Deliverables and technical descriptions provided in Attachments 3 and 4 we found the following details missing from the budget guidance and want to ensure we are budgeting for these accurately – should these be included in the budget instructions: a. Development- stage deliverables 'wet cell paste' and 'purified protein for assay development' are described in the technical section but are not in the table of Deliverables. b. Delivery of assay qualification protocols and reports. c. cGMP-compliant storage of the MCB for 2 years should be a deliverable.	Attachment 5 provides a series of cost assumptions and deliverables that are to be combined with the scope and deliverables provided in sample task orders. The offeror should assess the entire Sample Task Order, identify assumptions, determine the best path forward, provide rationale, and then provide the proposal based on this assessment. The offeror should include costs as appropriate.
27.	In Attachment 5, on page 6 of the Attachment, we are provided with guidance on how to budget for Sample Task Order 4. When comparing the Sample Task Order Deliverables and technical descriptions provided in Attachments 3 and 4 we found the following details missing from the budget guidance and want to ensure we are budgeting for these accurately – should these be included in the budget instructions: a. non-cGMP BDS for lyophillization studies are missing. b. Manufacturing plans + Gantt chart for BDS and adjuvant are missing. c. Master specification sheet is missing.	Attachment 5 provides a series of cost assumptions and deliverables that are to be combined with the scope and deliverables provided in sample task orders. The offeror should assess the entire Sample Task Order, identify assumptions, determine the best path forward, provide rationale, and then provide the proposal based on this assessment. The offeror should include costs as appropriate.

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	d. cGMP storage of BDS and adjuvant for 2 years should be a deliverable.	
28.	Will there be a requirement to manufacture BSL3/4 agents?	Please see the definition of "Other Biologic."
29.	Whether the submission of an RFP is restricted to manufacturers based in the United States, and whether manufacturers based in the US would be preferentially evaluated.	p. FAR Clause **52.225-1, Buy American--Supplies** (May 2014) is deleted in its entirety and FAR Clause **52.225-5, Trade Agreements** (October 2016) is substituted therefor. Notably, the following countries are NOT TAA eligible or compliant at this time: Russia India China Pakistan Malaysia Indonesia Iraq Iran Sri Lanka
30.	We ask therefore whether our proposal needs to be cast in terms of a specific proposal for a non-enveloped DS DNA virus or whether we might submit a proposal for a hepatitis A vaccine which makes use of novel cell substrates and strains making certain to illustrate our expertise	Offeror should respond to task orders and sample task orders as they are written. Additional expertise may be described within the appropriate task area section of the proposal.

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	and manufacturing capability according to the statement below. *The Contractor shall provide NIAID with a broad and flexible range of manufacturing and* *characterization services for vaccines and other biologics that support preclinical, nonclinical, and clinical studies for promising products when such products emerge from investigator-initiated research studies or other sources identified by NIAID Program staff.*	